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We Claim:

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1. A novel pyrrolo[2,1-c][1,4]benzodiazepine of formula IX where n is 3 to 10.

5 2. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

3. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

4. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

5. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

6. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

20 7. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

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8. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

9. A novel pyrrolobenzodiazepine as claimed in claim 1 of the structure

10. A process for the preparation of bis 2-fluoro pyrrolo[2,1-c][1,4]benzodiazepines of formula IX

Formula IX

where n is 3 to 10, which comprises:

- (a) reacting methyl (2S)-N-[4-benzyloxy-5-methoxy-2-nitrobenzoyl]-4-hydroxypyrrolidine-2-carboxylate dissolved in an organic solvent,
- (b) cooling the solution and adding a solution of diethylaminosulfurtrifluoride (DAST) in an organic solvent drop wise;
- (c) isolating the methyl (2S)-N-[4-benzyloxy-5-methoxy-2-nitrobenzoyl]-4-fluoropyrrolidine-2-carboxylate with DIBAL-H formed in the presence of an organic solvent and cooling;
- (d) isolating methyl (2S)-N-[4-benzyloxy-5-methoxy-2-nitrobenzoyl]-4-fluoropyrrolidine-2-carboxaldehyde formed;
- (e) protecting methyl (2S)-N-[4-benzyloxy-5-methoxy-2-nitrobenzoyl]-4-fluoropyrrolidine-2-carboxaldehyde with EtSH in presence of an organic solvent;
- (f) isolating (2.5)-N-[4-benzyloxy-5-methoxy-2-nitrobenzoyl]-4-fluoropyrrolidine-2-carboxaldehyde diethylthioacetal;

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(g) reacting the (2S)-N-[4-benzyloxy-5-methoxy-2-nitrobenzoyl]-4-fluoropyrrolidine-2-carboxaldehyde diethylthioacetal with a debenzylating agent to obtain (2S)-N-[4-hydroxy - 5 - methoxy - 2 - nitrobenzoyl] - 4 - fluoropyrrolidine - 2 - carboxaldehyde - diethylthioacetal of formula VI,

Formula VI

(h) reacting (2S)-N-[4-hydroxy-5-methoxy-2-nitrobenzoyl]-4-fluoro-2-carboxaldehyde diethylthioacetal of formula VI with a dibromoalkane in an aprotic water miscible organic solvent and in the presence of a mild inorganic base up to refluxing temperature and isolating 1,1'-{[(alkane-1,N-diyl)dioxy}bis[(2-nitro-5-methoxy-1,4-phenylene) carbonyl] bis [4-fluoropyrrolidin-2-carboxaldehyde diethylthioacetal] of formula VII where n is 3-10

Formula VII

(i) reducing the compound of formula VII with SnCl₂ .2H₂O in presence of organic solvent up to a reflux temperature and isolating 1,1'-{[(alkane-1,N-diyl)dioxy}bis[(2-amino-5-methoxy-1,4-phenylene)carbonyl]]bis [4-fluoro-pyrrolidin-2-carboxaldehyde diethylthioacetal]] of formula VIII where n is 3-10

Formula VIII

(j) reacting the compound of formula VIII with a deprotecting agent to obtain bis 2-fluoro pyrrolo[2,1-c][1,4]benzodiazepines of formula IX wherein n is as stated above.

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- 11. A process as claimed in claim 10 wherein the organic solvent used in steps (a), (b) and (c) comprises CH₂Cl₂.
- 12. A process as claimed in claim 10 wherein in step (a) the solution is cooled to a temperature of -78°C.
- 5 13. A process as claimed in claim 10 wherein the drop wise addition in step (b) is carried out for a period of 40 min.
 - 14. A process as claimed in claim 10 wherein step (c) is carried out after 15 hours of step (b).
- 15. A process as claimed in claim 10 wherein the cooling in step (c) is done to a temperature of -78°C and for a period of 45 minutes.
 - 16. A process as claimed in claim 10 wherein step (e) is carried out in presence of an organic solvent and at room temperature.
 - 17. A process as claimed in claim 10 wherein the the (25)-N-[4-hydroxy-5-methoxy-2-nitrobenzoyl]-4-fluoro-2-carboxaldehyde diethylthioacetal of formula VI is reacted with a dibromoalkane in an aprotic water miscible organic solvent selected from the group consisting of acetone, acetonitrile and DMF and in the presence of a mild inorganic base selected from the group consisting of K₂CO₃, C₅CO₃ and BaCO₃.
 - 18. A process as claimed in claim 10 wherein step (h) is carried out for a period of about 48 hours.
 - 19. A process as claimed in claim 10 wherein the reduction in step (i) is carried out in the presence of an organic solvent comprising methanol.
 - 20. A process as claimed in claim 10 wherein the deprotecting agent comprises a combination of HgCl₂ and HgO in CH₃CN/H₂O.
- 25 21. A process for the preparation of bis 2-fluoro pyrrolo[2,1-c][1,4]benzodiazepines of formula IX

Formula IX

where n is 3 to 10, which comprises:

(a) (2S)-N-[4-hydroxy - 5 - methoxy - 2 - nitrobenzoyl] - 4 - fluoropyrrolidine - 2 - carboxaldehyde - diethylthioacetal of formula VI,

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Formula VI

(b) reacting (2S)-N-[4-hydroxy-5-methoxy-2-nitrobenzoyl]-4-fluoro-2-carboxaldehyde diethylthioacetal of formula VI with a dibromoalkane in an aprotic water miscible organic solvent and in the presence of a mild inorganic base up to refluxing temperature and isolating 1,1'-{[(alkane-1,N-diyl)dioxy}bis[(2-nitro-5-methoxy-1,4-phenylene) carbonyl] bis [4-fluoropyrrolidin-2-carboxaldehyde diethylthioacetal] of formula VII where n is 3-10

Formula VII

(c) reducing the compound of formula VII with SnCl₂ .2H₂O in presence of organic solvent up to a reflux temperature and isolating 1,1'-{[(alkane-1,N-diyl)dioxy}bis[(2-amino-5-methoxy-1,4-phenylene)carbonyl]]bis [4-fluoro-pyrrolidin-2-carboxaldehyde diethylthioacetal]] of formula VIII where n is 3-10

Formula VIII

- (d) reacting the compound of formula VIII with a deprotecting agent to obtain bis 2-fluoro pyrrolo[2,1-c][1,4]benzodiazepines of formula IX wherein n is as stated above.
- 22. A process as claimed in claim 21 wherein the (25)-N-[4-hydroxy-5-methoxy-2-nitrobenzoyl]-4-fluoro-2-carboxaldehyde diethylthioacetal of formula VI is reacted with a dibromoalkane in an aprotic water miscible organic solvent selected from the group consisting of acetone, acetonitrile and DMF and in the

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- presence of a mild inorganic base selected from the group consisting of K_2CO_3 , $CsCO_3$ and $BaCO_3$.
- 23. A process as claimed in claim 21 wherein step (b) is carried out for a period of about 48 hours.
- 5 24. A process as claimed in claim 21 wherein the reduction in step (c) is carried out
 / in the presence of an organic solvent comprising methanol.
 - 25. A process as claimed in claim 21 wherein the deprotecting agent comprises a combination of HgCl₂ and HgO in CH₃CN/H₂O.
- 26. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of formula IX and pharmaceutically acceptable additives.
 - 27. Method for the treatment of cancer in a patient suffering from the same, said method comprising administering to the patient a pharmaceutically effective amount of a compound of formula IX.
 - 28. A method as claimed in claim 27 wherein the patient is a mammal.
- 15 29. A method as claimed in claim 27 wherein the mammal is a human being.
 - 30. A method as claimed in claim 27 wherein the cancer is selected from the group consisting of leukemia, non-small cell, lung, colon, CNS, melanoma, ovarian, renal, prostate and breast.
- 31. Use of a compound of formula IX for the treatment of cancer selected from the group consisting of leukemia, non-small cell, lung, colon, CNS, melanoma, ovarian, renal, prostate and breast in a subject suffering from the same.

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